

Serial No.: 10/849,606 Examiner: Aulakh, Charanjit Filed: 05/20/04 Art Unit: 1625

Applicant: Stefan Kwiatkowski

Title:Fluorinated Heterocyclic Compounds and Methods of Synthesis

Atty. Docket No.: CUTLER-08582 Sheet 1 of 8

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FIG. 1A

FIG. 1B

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Methods of Synthesis

Atty. Docket No.: CUTLER-08582 Sheet 2 of 8

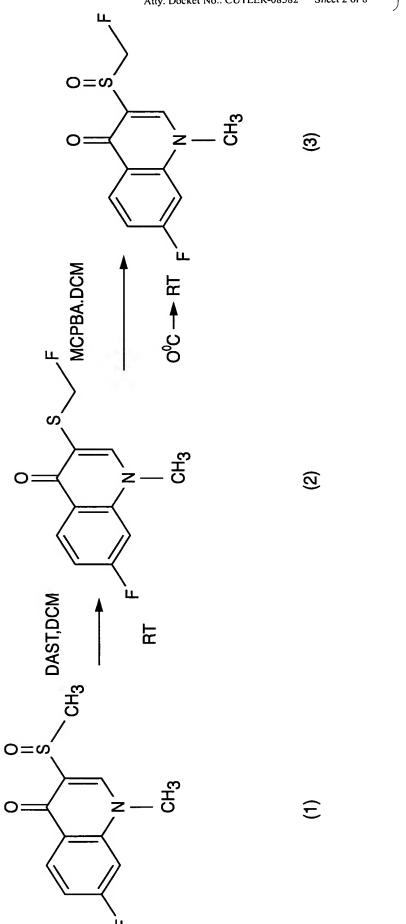


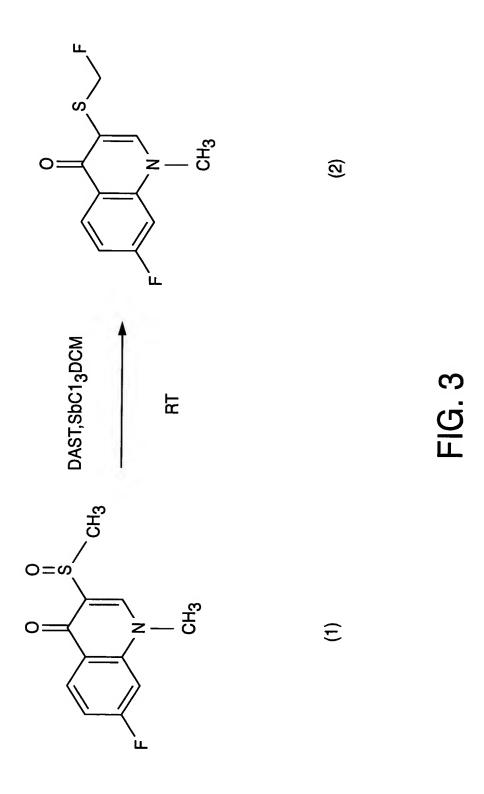
FIG. 2

Filed: 05/20/04 Art Unit: 1625 Serial No.: 10/849,606 Examiner: Aulakh, Charanjit

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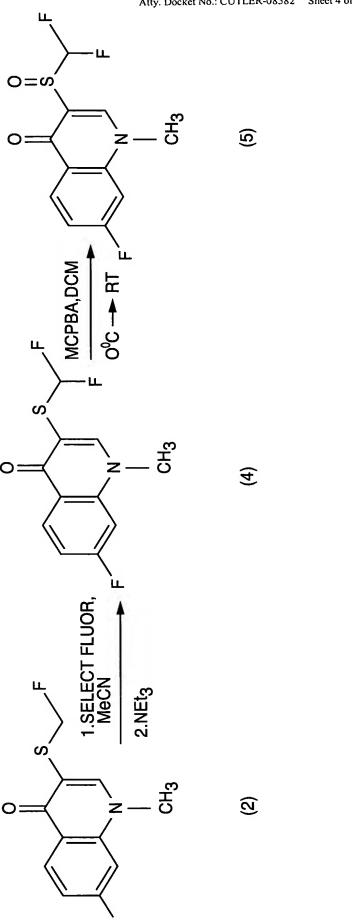
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Methods of Synthesis
Atty. Docket No.: CUTLER-08582 Sheet 3 of 8



Serial No.: 10/849,606 Filed: 05/20/04 Examiner: Aulakh, Charanjit Art Unit: 1625 Applicant: Stefan Kwiatkowski Title: Fluorinated Heterocyclic Compounds and Filed: 05/20/04 Art Unit: 1625

Methods of Synthesis
Atty. Docket No.: CUTLER-08582 Sheet 4 of 8



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Atty. Docket No.: CUTLER-08582 Sheet 5 of 8

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Š.				Mµ00	00µM	00µM	100µM	MH001	MH00				MH	300µM	100µM		MI				LM T	μM
CO				100	5	100	100	5	5		1000µM		1000µM	300	100		2 1000µM		1000µM		1000µM	1000µМ
<u>"</u>				2	0	α	N	0	N		N		α	N	0		N		N		N	7
SPP				bov	hum	hum	hum	hum	bov		hum		rat	rat			rat		rat		rat	rat
BATCH* SPP. n= CONC. † %INHIBITION				45373	45375	45376	45253	45452	45453		45273		45090	45491			45139		45167		45262	45039
				PHOSPHODIESTERASE PDE1	PHOSPHODIESTERASE PDE2	PHOSPHODIESTERASE PDE3		PHOSPHODIESTERASE PDE5	PHOSPHODIESTERASE PDE6	PROTEIN SERINE/THREONINE	*	178010 PROTEIN SERINE/THREONINE	KINASE PKC, NON-SELECTIVE			YPE L,		YPE L,		YPE L,		INOSITOL TRIPHOSPHATE IP3
TARGET				STERAS	STERAS	STERAS	STERAS	STERAS	STERAS	NE/THE	KINASE PKCa	INE/TH	NON-SE			214510 CALCIUM CHANNEL TYPE L,	BENZOTHIAZEPINE	214600 CALCIUM CHANNEL TYPE L,	DIHYDROPYRIDINE	215000 CALCIUM CHANNEL TYPE L,	PHENYLALKYLAMINE	PHOSPI
Δ					밀으		るのに			N SEF	KINAS	N SEF	PKC,			M CH/	IZOTI-	M CH/	YDRO	M CH	YLA	LTRI
				HOSPF	HOSPH	HOSPF	HOSPF	HOSPF	HOSPF	ROTEI		ROTEIL	INASE			ALCIUN	BEN	ALCIUN	ΩH	ALCIUN	PHE	IOSITO
 .												G G	¥			C)		C		C)		
CAT.#				146000	148000	152000	154000	156000	156100	180010		17801(•	•	•	21451(21460(21500(242500
														•	▼			_		-		

BATCH: REPRESENTS COMPOUNDS TESTED CONCURRENTLY IN THE SAME ASSAY(S).

RESULTS WITH≥50% STIMULATION OR INHIBITION ARE BOLDFACED. **◆DENOTES ITEM MEETING CRITERIA FOR SIGNIFICANCE**

(NEGATIVE VALUES CORRESPOND TO STIMULATION OF BINDING ENZYME ACTIVITY) bov=BOVINE; hum=HUMAN R=ADDITIONAL COMMENTS

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Atty. Docket No.: CUTLER-08582 Sheet 6 of 8

Serial No.: 10/849,606 Filed: 05/20/04
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Applicant: Stefan Kwiatkowski
Title: Fluorinated Heterocyclic Compounds and
Methods of Synthesis
Atty. Docket No.: CUTLER-08582 Sheet 7 of 8

1									
CAT.#	TARGET	BATCH* SPP. n= CONC.	SPP.	n= C	ONC.	†%INHIBITION	Z		IC ₅₀
						-100 -50	0 50	100	}
						→ → %	→	-	
Р (146000 PHOSPHODIESTERASE PDE1	47821	pov	T-	Mµ000	50			
		48192	pov	_	000µM	55		•	385µM
				7	00µM	45			
				N	10µM	17			
				8	1µM	12			
148000 PF	PHOSPHODIESTERASE PDE2	47677	hum	9	00µM	-2			
152000 PH	4OSPHODIESTERASE PDE3	47676	hum	2 10	000µM	99			
		48194	hum	_	000µM	55		-	418µM
				2	00µM	44			-
				ر د	10µM	9	_	-	
				Q	1 TrW	<u>-</u>			
	PHOSPHODIESTERASE PDE4	47675	hum	_	000µM	25			
	1OSPHODIESTERASE PDE5	47674	hum	•	1000µM	28		_	
156100 PF	PHOSPHODIESTERASE PDE6	47672	oq Q	2 10	000µM	24			
178010 PF	PROTEIN SERINE/THREONINE								
玄	KINASE PKC, NON-SELECTIVE	47916	rat	_	000mM	64			
		48199	rat	_	000µM	57			644µM
				_	00µM	24		•	-
					10µM	0			
				2	1 TM	-5			
1									

FIG. 8

385µM 644µM **IC50** 100 **†**%INHIBITION -50 -100 20 44 25 28 24 24 % 55 100µM 10µM 000µM 000µM 10_{LM} 1 M T T Σď MU000 100µM 10µM 100 LM 1000LM 000 MM 1000LM BATCH SPP. n= CONC. 20000 2000 2000 hum hov bov hum hum <u></u>8 po oo ā ā 47916 48199 48192 47676 47675 47674 47672 48194 47821 47677 KINASE PKC, NON-SELECTIVE PROTEIN SERINE/THREONINE PHOSPHODIESTERASE PDE4 PHOSPHODIESTERASE PDE5 PHOSPHODIESTERASE PDE6 PHOSPHODIESTERASE PDE2 PHOSPHODIESTERASE PDE3 ◆ 146000 PHOSPHODIESTERASE PDE1 **TARGET** 152000 156000 156100 178010 154000 148000 CAT.#

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